

What is claimed is:

1. Nucleic acid, the sequence of which comprises SEQ ID No: 1.
2. Nucleic acid of clone fohd013a05m, ATCC Deposit No. 98409.
3. Nucleic acid, the sequence of which comprises a sequence complementary to SEQ ID No: 1 or to a unique fragment thereof.
4. Nucleic acid of claim 3 that is ribonucleic acid (RNA).
5. Nucleic acid, the sequence of which comprises a sequence at least 50% identical to SEQ ID No: 1.
6. Nucleic acid that hybridizes to SEQ ID No: 1 or to the complement thereof.
7. Nucleic acid of claim 6 that hybridizes under stringent conditions.
8. Nucleic acid, the sequence of which comprises a degenerate sequence variant of SEQ ID No:1.
9. Nucleic acid encoding a polypeptide, the amino acid sequence of which comprises SEQ ID No: 2.
10. Nucleic acid encoding a polypeptide, the amino acid sequence of which comprises a sequence sharing at least 75% sequence similarity with SEQ ID No: 2.
11. An oligonucleotide that hybridizes to a unique fragment of the nucleic acid of claim 10.
12. An oligonucleotide of claim 11 that hybridizes under stringent conditions.
13. An oligonucleotide of claim 11 that hybridizes under intracellular conditions.

14. An oligonucleotide of claim 11 comprising at least one modification in a nucleotide base, backbone sugar, phosphate or sugar-phosphate linkage.
15. A modified oligonucleotide of claim 14 comprising a peptide nucleic acid backbone.
16. A detectably labeled oligonucleotide of claim 11.
17. A biotinylated, radiolabeled or fluorophore-conjugated oligonucleotide of claim 16.
18. An oligonucleotide of claim 11 wherein said unique fragment is at least 9 nucleotides in length.
19. An oligonucleotide of claim 11 wherein said unique fragment is at least 15 nucleotides in length.
20. An oligonucleotide of claim 11 wherein said unique fragment is at least 21 nucleotides in length.
21. An oligonucleotide of claim 11 wherein said unique fragment is a locus comprising a 5' untranslated sequence, transcription initiation site, coding sequence, intron-exon boundary, polyadenylation site, or 3' untranslated sequence in the nucleic acid of claim 10.
22. An oligonucleotide, the sequence of which is selected from the group consisting of SEQ ID Nos: 4, 5, 6, 7 and 8.
23. An antisense vector comprising nucleic acid encoding an oligonucleotide of claim 11.

24. An antisense pharmaceutical composition comprising an oligonucleotide of claim 11 or a vector of claim 23 dispersed in a pharmaceutically acceptable vehicle.

25. An MRP- β polypeptide, the amino acid sequence of which comprises SEQ ID No: 2.

26. An MRP- β polypeptide, the amino acid sequence of which comprises a sequence sharing at least 75% sequence similarity with SEQ ID No: 2.

27. An epitope unique to the MRP- β polypeptide of claim 26.

28. An epitope of claim 27 that is displayed by a cell expressing an MRP- β gene.

29. An antibody that binds selectively to the epitope of claim 27.

30. An antigen-binding fragment of the antibody of claim 29.

31. A fusion polypeptide comprising an antigen-binding fragment of claim 30.

32. A fusion polypeptide of claim 31, further comprising a cytotoxic polypeptide, such that said fusion polypeptide stimulates cytolysis of a cell expressing an MRP- β gene.

33. A fusion polypeptide of claim 31, further comprising a chemoattractant, such that said fusion polypeptide stimulates destruction of a cell expressing an MRP- β gene by macrophages, killer T cells or cytotoxic T cells.

34. An expression vector comprising nucleic acid encoding the polypeptide of claim 26.

35. A cell transfected with an expression vector of claim 34.

36. A cell of claim 35 that is immortalized under cell culture conditions.

37. A cell of claim 36 that is of human origin.

38. A cell of claim 36 that is a unicellular organism.

39. A yeast cell of claim 38.

40. A cell of claim 35 that is a non-human mammalian embryonic blastocyst cell.

41. A non-human mammal produced by intrauterine implantation of a blastocyst comprising the cell of claim 40

42. Progeny of the mammal of claim 41, said progeny characterized by germline integration of said nucleic acid encoding the MRP- β polypeptide of claim 25.

43. A null vector comprising nucleic acid encoding a non-expressible variant of the polypeptide of claim 26.

44. A cell transfected with the null vector of claim 43.

45. A cell of claim 44 that is a non-human mammalian embryonic blastocyst cell.

46. A non-human mammal produced by intrauterine implantation of a blastocyst comprising the cell of claim 45.

47. Progeny of the mammal of claim 46, said progeny characterized by germline integration of nucleic acid encoding a non-expressible variant of the polypeptide of claim 26.

48. A method of detecting a mutation in an MRP- β gene, comprising the steps of:

(a) obtaining cellular tissue from a mammal suspected of harboring a variant MRP- β gene, the sequence of which differs from SEQ ID No: 1 by at least one nucleotide substitution, insertion or deletion;

(b) releasing nucleic acids from said cellular tissue;

(c) combining, under hybridization conditions, said released nucleic acids with an oligonucleotide complementary to SEQ ID No: 1 or to a unique fragment thereof; and

(d) assaying said released nucleic acids for formation of a hybrid comprising said oligonucleotide, formation of which indicates that said mammal harbors at least one wild-type MRP-β gene allele, the sequence of which comprises SEQ ID No: 1.

49. A method of detecting expression of an MRP-β gene, comprising the steps of:

(a) obtaining cellular tissue from a mammal suspected of harboring cells expressing an MRP-β gene encoding a polypeptide of claim 25;

(b) releasing RNA from said cellular tissue;

(c) combining, under hybridization conditions, said released RNA with an oligonucleotide that hybridizes to the complement of SEQ ID No: 1 or a unique fragment thereof, and

(d) assaying said released RNA for formation of a hybrid comprising said oligonucleotide, formation of which indicates that cells of said tissue express said MRP-β gene.

50. The method of claim 48 or 49 wherein said cellular tissue is suspected of comprising transformed cells.

51. A method of characterizing multidrug-resistant phenotype of a transformed cell of mammalian origin, comprising the steps of:

- (a) obtaining cellular tissue from a mammal suspected of harboring transformed cells;
- (b) releasing RNA from said cellular tissue;
- (c) combining, under hybridization conditions, said released RNA with an oligonucleotide that hybridizes to the complement of SEQ ID No: 1 or a unique fragment thereof; and
- (d) assaying said released RNA for formation of a hybrid comprising said oligonucleotide, formation of which indicates presence of transformed cells having a multidrug-resistance phenotype.

52. The method of claim 48, 49 or 51 wherein said oligonucleotide comprises a peptide nucleic acid backbone.

53. A method of characterizing drug-resistant phenotype of a transformed cell of mammalian origin, comprising the steps of:

- (a) obtaining cellular tissue from a mammal suspected of harboring transformed cells;
- (b) contacting said tissue with an antibody of claim 29, under conditions such that, if cells of said tissue display said an epitope selectively bound by said antibody, an antibody-epitope complex forms; and,
- (c) assaying said tissue for the presence of said complex, formation of which indicates presence of transformed cells having a drug-resistant phenotype in said mammal.

54. The method of claim 51 or 53 wherein said cellular tissue is of mammary, respiratory tract, urogenital tract, endocrine system or immune system origin.

55. The method of claim 54 wherein said cellular tissue is of mammary origin and comprises a breast biopsy sample.

56. The method of claim 54 wherein said cellular tissue is of respiratory tract origin and comprises a bronchoalveolar lavage sample.

57. The method of claim 54 wherein said cellular tissue is of urogenital tract origin and comprises an ovarian, uterine or cervical biopsy sample.

58. The method of claim 54 wherein said cellular tissue is of urogenital tract origin and comprises a prostate or testicular biopsy sample.

59. The method of claim 54 wherein said cellular tissue is of endocrine system origin and comprises a pancreatic biopsy sample.

60. The method of claim 54 wherein said cellular tissue is of immune system origin and comprises a spleen, bone marrow or lymph node biopsy sample.

61. A method of mitigating aberrant expression of an MRP- β gene, comprising the step of:
administering an antisense pharmaceutical composition of claim 24 to a mammal suffering from effects of said aberrant expression, under conditions sufficient to attenuate a phenotype associated therewith.

62. A method of mitigating aberrant activity of an MRP- β gene, comprising the step of:
administering an antisense pharmaceutical composition of claim 24 to a mammal suffering from effects of said aberrant activity, under conditions sufficient to attenuate a phenotype associated therewith.

63. A method of improving effectiveness of chemotherapy for a mammal afflicted with a multidrug-resistant tumor, comprising the steps of:

- administering a chemotherapeutic drug to said mammal; and,
- coadministering an antisense pharmaceutical composition of claim 24, such that said antisense pharmaceutical composition mitigates resistance of said tumor to said chemotherapeutic drug.

64. A method of treating a mammal suffering from aberrant expression of an MRP- β gene, comprising the step of administering a fusion polypeptide of claim 32 or 33 to said mammal, in an amount effective for destroying cells aberrantly displaying an epitope of claim 27.

65. A method of treating a mammal suffering from aberrant activity of an MRP- β polypeptide, comprising the step of administering a fusion polypeptide of claim 32 or 33 to said mammal, in an amount effective for destroying cells aberrantly displaying an epitope of claim 27.

66. A method of treating a mammal afflicted with a multidrug-resistant tumor, comprising the step of administering a fusion polypeptide of claim 32 or 33 to said mammal, in an amount effective for destroying tumor cells displaying an epitope of claim 27.

67. A method of identifying a modulator of MRP- β , comprising the steps of:

- contacting a cell of claim 35 with a candidate modulator of MRP- β ;
- assaying the level of MRP- β gene expression in said cell, wherein a detectable fluctuation in said level indicates that said candidate is an MRP- β modulator.

68. A method of identifying a modulator of MRP- β , comprising the steps of:

- (a) contacting a cell of claim 35 with a candidate modulator of MRP- β ;
- (b) assaying the level of MRP- β polypeptide displayed by said cell, wherein a detectable fluctuation in said level indicates that said candidate is an MRP- β modulator.

69. A method of identifying a modulator of MRP- β , comprising the steps of:

- (a) contacting a cell of claim 35 with a substrate transported by MRP- β ;
- (b) contacting a cell of claim 35 with a candidate modulator of MRP- β ;
- (c) assaying the amount of said substrate exported by said cell, wherein a detectable fluctuation in said amount indicates that said candidate is an MRP- β modulator.

70. A method of identifying a modulator of MRP- β , comprising the steps of:

- (a) contacting a cell of claim 35 with a cytotoxin exported or sequestered by MRP- β ;
- (b) contacting a cell of claim 35 with a candidate modulator of MRP- β ;
- (c) assaying survival of said cell, a detectable fluctuation in which indicates that said candidate is an MRP- β modulator.

71. A method of identifying a modulator of MRP- β , comprising the steps of:

- (a) contacting a cell of claim 35 with a cytotoxin exported by MRP- β ;
- (b) contacting a cell of claim 35 with a candidate modulator of MRP- β ;

(c) assaying efflux of said cytotoxin from said cell, a fluctuation in which indicates that said candidate is an MRP- β modulator.

72. An MRP- β modulator identified by the method of claim 67, 68, 69, 70 or 71.

73. An MRP- β modulator of claim 72 that is an inhibitor.

74. An MRP- β modulator of claim 72 that is a small molecule.

75. A multidrug-resistance attenuating pharmaceutical composition comprising a modulator of claim 72 dispersed in a pharmaceutically acceptable vehicle.

76. A method of mitigating aberrant expression of an MRP- β gene, comprising the step of administering an MRP- β modulator to a mammal suffering from effects of said aberrant expression, under conditions sufficient to attenuate a phenotype associated therewith.

77. A method of treating a mammal suffering from aberrant activity of an MRP- β polypeptide, comprising the step of administering an MRP- β modulator to a mammal suffering from effects of said aberrant activity, under conditions sufficient to attenuate a phenotype associated therewith.

78. A method of improving effectiveness of chemotherapy for a mammal afflicted with a multidrug-resistant tumor, comprising the steps of:

(a) administering a chemotherapeutic drug to said mammal; and,

(b) coadministering a pharmaceutical composition of claim 75,

such that said composition mitigates resistance of said tumor to said chemotherapeutic drug.

79. The method of claim 78 wherein said tumor is of mammary, respiratory tract, urogenital tract, endocrine system or immune system origin.

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* C2